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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/460,920	12/14/1999	BETH ANNE PIPER	LA0046A	3115

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EXAMINER	
ZHANG, NANCY L	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	09/460,920	PIPER, BETH ANNE	
	Examiner	Art Unit	
	Nancy L. Zhang	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,45-54,58-60,71-73 and 75-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,45-54,58-60,71-73 and 75-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and arguments filed on August 8, 2006 have been received.

In view of applicant's amendment, the claim objection of claim 48 is hereby withdrawn.

Applicant's arguments with respect to the rejection under 35 USC § 103 as being unpatentable over Whitcome (US Patent 6,011,049) along with submitted affidavits, have been considered but are moot in view of the new ground(s) of rejection.

Claims 37, 45-54, 58-60, 71-73, and 75-79 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 45-54, 58-60, 71-73, and 75-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "drug naïve patient" renders the claims indefinite because the claim includes elements not actually disclosed which could mean the "drug naïve patient" is "a patient who has not received any drug", thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d). The "type 2 diabetes" in the preamble of the claims may be implied as being what is meant for the "drug" of treatment but this is

implied at best. An implied limitation is not clear and concise as required under 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37, 45-54, 58-60, 71-73, and 75-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barelli et al.(WO 97/17975, pub date: May 22, 1997, equivalent to US Patent 5,922,769) in view of Bauer et al. (US Patent 5,258,185, issue date: Nov. 2, 1993).

Claims 37, 45-54, 58-60, 71-73, and 75-79 are directed to a method of treating type 2 diabetes comprising administering to a drug naïve human patient, as first line therapy, a low dose of a combination of metformin and glyburide where the daily dosage of metformin is about 160 mg to about 750 mg; the daily dosage of glyburide is about 0.5 mg to 15 mg. Further limitations include: metformin and glyburide is formulated as a single dosage form (claim 45); weight ratio of metformin and glyburide is from about 400:1 to about 50:1 (claim 46); and that the glyburide having particular particle distributions and the patient population being drug naïve patients as recited in the claims.

Barelli et al. teach a combination of 500 mg metformin and 5 mg glibenclamide (glibenclamide and glyburide are synonymous) being useful for the treatment of type II diabetes (column 3, lines 14-17) and that the combination makes the therapeutical effect optimum at any time of the progression of the disease, starting from minor cases to the most severe ones (column 3, lines 19-21). Barelli et al. also disclose that the weight ratio of metformin and glibenclamide is 200:1 (column 2, lines 18-20) which overlaps with the claimed weight ratio. Barelli et al. further teach a single coated tablet in EXAMPLE 1 (column 9, lines 25-26) which contains 500 mg metformin and 5 mg glibenclamide.

The difference between Barelli et al.'s teaching and the instant claimed invention lies in that Barelli et al. do not teach (i) glyburide having particular particle distributions and (ii) the patient population being drug naïve patients.

However, Bauer et al. teaches pharmaceutical formulations of glibenclamide rapidly releasing the active substance for the treatment of diabetes (see abstract). Bauer et al. disclose improved drug release and bioavailability (column 2, lines 17-22) of the drug glibenclamide by using a preparation having micronized glibenclamide with mean particle size of ± 5 μm which overlaps with the instantly claimed particle size of 2-60 μm. Therefore, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to prepare micronized glibenclamide for the combination of metformin and glibenclamide as disclosed by Barelli et al. in view of Bauer et al. to result in the drug combination of the instant invention, motivated by Bauer et al. that

glibenclamide is virtually water-insoluble (column 2, line 9) and micronized glibenclamide improves its solubility and bioavailability (column 2, lines 31-32).

With regard to the patient population, although Barelli et al. do not explicitly teach that the combination is administered to a drug naïve patient as a first line therapy, Barelli et al. do disclose that the combination makes the therapeutical effect (for treating type 2 diabetes) optimum at any time of the progression of the disease, starting from minor cases to the most severe ones (column 3, lines 19-21). Since the patient population of Barelli et al.'s method of treatment is type 2 diabetic, without identifying a patient's drug status and treatment history, one having ordinary skill in the art still would have been motivated to treat the patient with Barelli et al.'s combination of metformin and glyburide.

Therefore, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the treatment of Barelli et al. in view of Bauer et al. to result in the practice of the instant invention with a reasonable expectation of success.

With respect to the recitation of "lowering blood glucose in a hyperglycemic human patient", "decreasing insulin resistance, decreasing hemoglobinA1c, increasing post-prandial insulin levels or decreasing prandial glucose excursion" in claims 71 and 72, since the drug combination of metformin and glyburide is the same as what's disclosed in the prior art and are being administered to the same patient population, the recited effects are expected and thus do not limit the claims.

With respect to the recitation of claim 54 regarding patient baseline measurements, those values are the same as those measured for the type 2 diabetic patient as disclosed by Barelli et al. (column 4, lines 23-29).

With respect to the recitation of metformin dosage being 250 mg, glyburide dosage being 1.25 mg of claims 50, 53, 54, 58, 59 and 79, although Barelli et al. do not explicitly teach this particular dosage, Barelli et al. have provided guidance that 1500 mg metformin and 15 mg glyburide are the maximum recommended daily dosage in the combination (column 3, lines 37-40) with recommended weight ratio of 200:1 (column 2, line 20) between metformin and glyburide. The determination of the appropriate dosage amounts of active ingredients for a treatment is routinely made by those of ordinary skill in the art and is well within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information of the active ingredient disclosed in the prior art. Thus, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to determine the amount of metformin and the amount of glyburide for achieving the effect of treating type 2 diabetes to result in the pharmaceutical composition as claimed with a reasonable expectation of success.

Applicant's attention is further drawn to MPEP at §2144.05, which states, "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage range is the optimum combination of percentages... where the general condition of a claim are

disclosed in the prior, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23 and 44 of U.S. Patent No. 6,660,300. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented invention makes obvious the instant invention.

The patented invention is directed to a method of administering the same combination of metformin and glyburide as that of the instantly claimed invention for treating diabetes which includes overlapping patient population of the type 2 diabetic

patients in the instant invention. Therefore, the patented invention makes obvious the instant invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy L. Zhang whose telephone number is (571)-272-8270. The examiner can normally be reached on Mon.- Fri. 8:30am - 5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NLZ 1/5/07

NLZ

BRIAN YONG S KWON
PRIMARY EXAMINER